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EXAMINER	
HUANG, GIGI GEORGIANA	
ART UNIT	PAPER NUMBER
1612	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,154	KLOBCAR ET AL.	
	Examiner	Art Unit	
	GIGI HUANG	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *1-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/17/2006, 7/11/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II in the reply filed on April 28, 2008 is acknowledged. The traversal is on the ground that the special technical feature shared by all the claims is a composition comprising perindopril or a salt thereof, preferably comprising at least one inorganic carbonate, more preferably comprising indapamide produced by dry mixing. This is not found persuasive because the claims as written for Group I are to a method of making a composition comprising perindopril or a salt thereof with at least one inorganic carbonate, at least one carrier, by dry processing; While Group II is to a composition of perindopril or salt thereof comprising at least one of microcrystalline cellulose and anhydrous lactose. Claim 13 of Group II recites the carbonate as optional and is not specifically recited to be part of the composition. Thereby, the claims of Group I require perindopril with a carrier and a carbonate and Group II requires perindopril with microcrystalline cellulose or anhydrous lactose (carriers). The claims lack unity as a result. The argument of unity per the IPER is not persuasive as addressed above, the claims as written do not share unity other than perindopril or salt thereof with a carrier (e.g. cellulose) which as taught by Eyjolfsson.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application

2. Applicant has elected Group II in response to restriction requirement the examination.

Due to restriction, based on election of Group II, claims 1-12 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 13-17 are present for examination at this time.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim14, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. It is unclear and does not allow one of skill in the art to ascertain the metes and bounds of the invention. For purposes of prosecution, only the ratio of 0.1-0.9 is examined.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Guez et al. (WO 99/25374).

It is noted that Guez et al (U.S. Pat. 6653336) will be used as the translation for Guez et al. (WO 99/25374) and all references will be to the U.S. Pat.

Guez et al. teaches the combination of an angiotensin-converting enzyme inhibitor (ACE or CEI) and a diuretic in a pharmaceutical composition. Guez teaches the benefits of the combination and the preferred CEI particularly is perindopril and its salts. The preferred diuretic is indapamide and hydrochlorothiazide and their salts, more particularly indapamide. Examples teach the combination of perindopril and indapamide in pharmaceutical compositions with excipients including microcrystalline cellulose. Guez teaches the inclusion of excipients, binders, diluents, stabilizing agents, and other desirable components (Abstract, Col. 2 line 55-62, Col. 3 line 11-Col. 4 line 50). It is known in the art that microcrystalline cellulose is a moisture control agent and the commercially available products (such as Avicel®PH-101) generally have moisture contents of less than 5% (see Signet sheets). Guez also teaches several composition forms including instantaneous and delayed release.

All the critical elements are taught by the cited reference and thus the claims are anticipated.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guez et al. (WO 99/25374) as applied to claim 13 above, in view of www.signetchem.com, and further in view of Cooper et al. (U.S. Pat. Publication 2003/0232796).

The teachings of Guez et al. are addressed above.

Guez et al. do not expressly teach the use of microcrystalline cellulose with a moisture content of 0.3-1.5% by weight. Guez does teach the inclusion of microcrystalline cellulose and the diuretic indapamide. Guez also teaches several composition forms including instantaneous and delayed release.

www.signetchem.com teaches that a number of commercial microcrystalline celluloses with different properties, size, and forms were readily available for purchase and use in 2002 for one of skill in the art at the time of the invention to produce the product properties desired.

Cooper et al. teaches the use of nanoparticles of active agents with various particle sizes of other actives to obtain immediate-release and controlled-release forms. The actives include cardiovascular agents, cardiac inotropic agent, diuretic, and antihypertensive agents.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize any commercially available microcrystalline celluloses (e.g. Avicel®PH-112) and to modify the particle size of the drugs, in the

composition taught by Guez, as suggested by www.signetchem.com and Cooper, and produce the instant invention.

It would have been obvious at the time of the invention to purchase any appropriate microcrystalline cellulose such as Avicel®PH-112 to use and to modify the composition taught by Guez as needed to arrive at a final product with the desired properties. It would have also been obvious to modify the teachings of Guez including particle size, to create products with any number of specialized forms and applications (e.g. immediate release, delayed release, etc.) depending the on the drug release profile and form desired which is well within the skill of one in the art.

One of ordinary skill in the art would have been motivated to do this because it is more cost effective to purchase a commercial product than to produce the microcrystalline cellulose yourself, and the commercial product is desirable as it had consistent properties and uniformity in the mixture. One would have been motivated to modify the components (microcrystalline cellulose, particle size, etc.) to provide a number of materials that would be uniquely suited for the product use desired.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guez et al. (WO 99/25374) as applied to claim 13 above in view of Eyjolfsson (WO 03/059388).

The teachings of Guez et al. are addressed above.

Guez et al. do not expressly teach the use of a carbonate at a molar ratio of 0.1-0.9 for perindopril to inorganic carbonate. Guez does teach the inclusion of excipients such as stabilizing agents in the formulation.

Eyjolfsson teaches the inclusion of components including of carbonates, particularly alkali or alkaline-earth metal carbonates produce useful and stable ACE inhibitor formulations. The ACE inhibitors taught include perindopril and the combination of diuretics. Eyjolfsson also teaches a preferred embodiment of the amount of carbonate to at least the equivalent of the active.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to include carbonates, as suggested by Eyjolfsson, and produce the instant invention.

It would have been obvious at the time of the invention to incorporate components to increase stabilization of a formulation as taught by Guez such as the carbonates taught by Eyjolfsson for ACE inhibitors like perindopril. Although Eyjolfsson teaches a preferred embodiment wherein the amount of carbonate to at least the equivalent of the active, the teaching as a whole is to the inclusion of carbonates for the improved stabilization of ACE inhibitor and it would have been obvious to one of skill in the art to optimize the amount carbonate beyond the preferred range as the general teaching encompasses ratios below 1:1. Where the general conditions of a claim are

disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation as the adjustment of particular conventional working conditions, such as determining a suitable effective dosage in combination with other component ranges, is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

One of ordinary skill in the art would have been motivated to do this because combining components that would provide a more stable composition and yield an increasingly effective and desirable product with better shelf life is desirable.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

10. Claims 13-17 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GIGI HUANG whose telephone number is (571)272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fredrick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH
/Zohreh A Fay/
Primary Examiner, Art Unit 1612